

=====

Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Anne Corrigan

Timestamp: Thu Jun 07 20:19:22 EDT 2007

=====

\*\*\*\*\*

Reviewer Comments:

<210> 1  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> CodY target sequence

Please explain the source of "<223> CodY target sequence."

<210> 15  
<211> 8  
<212> PRT  
<213> Artificial Sequence  
<220>  
<223> consensus sequence GTP binding motif in CodY homologs  
<220>  
<221> Xaa  
<222> (2)..(2)  
<223> Arg  
<220>  
<221> Xaa  
<222> (3)..(3)  
<223> Met, Gly, Ile, Lys, Gln  
<220>  
<221> Xaa  
<222> (4)..(4)  
<223> Gly  
<220>

```
<221> Xaa
<222> (5)..(5)
<223> Thr
<220>
<221> Xaa
<222> (7)..(7)
<223> Ser
<400> 15
Gly Gly Glu Arg Leu Gly Thr Thr
1 5
```

There are no Xaa's at locations 2-4, and 5-7. Why are there Xaa explanations? e.g., "Gly" is at location 2--it can only represent itself; "Glu" is at location 3. Same type of error in Sequence 15.

```
<220>
<221> Variant
<222> (2)..(2)
<223> Ala, Lys
<220>
<221> Variant
<222> (3)..(3)
<223> Phe, Ile
<400> 24
Asp Arg Val Gly
1
```

The <222> and <223> responses above are invalid. "Arg" is at location 2--it can only represent itself. If you want location 2 to represent Arg, Ala, or Lys, please use "Xaa" instead of "Arg." Same problem with the <222> (3)..(3) and the <223> line below it.

Same type of error in Sequence 29.

```
<210> 226
<211> 30
<212> DNA
<213> Artificial Sequence
<220>
<223> MUT16
```

The <223> response above is an insufficient explanation for <213>

Artificial Sequence. Please give the source of "MUT16." Same type of error throughout the submitted file.

\*\*\*\*\*

Application No: 10562601 Version No: 1.0

### Input Set:

### Output Set:

**Started:** 2007-06-07 15:32:33.514  
**Finished:** 2007-06-07 15:32:36.262  
**Elapsed:** 0 hr(s) 0 min(s) 2 sec(s) 748 ms  
**Total Warnings:** 207  
**Total Errors:** 12  
**No. of SeqIDs Defined:** 234  
**Actual SeqID Count:** 234

**Input Set:**

**Output Set:**

**Started:** 2007-06-07 15:32:33.514  
**Finished:** 2007-06-07 15:32:36.262  
**Elapsed:** 0 hr(s) 0 min(s) 2 sec(s) 748 ms  
**Total Warnings:** 207  
**Total Errors:** 12  
**No. of SeqIDs Defined:** 234  
**Actual SeqID Count:** 234

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (24)
W 213	Artificial or Unknown found in <213> in SEQ ID (29)
W 213	Artificial or Unknown found in <213> in SEQ ID (39)
W 213	Artificial or Unknown found in <213> in SEQ ID (40)
W 213	Artificial or Unknown found in <213> in SEQ ID (41) This error has occurred more than 20 times, will not be displayed
E 257	Invalid sequence data feature in <221> in SEQ ID (214)
E 257	Invalid sequence data feature in <221> in SEQ ID (214)
E 257	Invalid sequence data feature in <221> in SEQ ID (214)
E 257	Invalid sequence data feature in <221> in SEQ ID (214)
E 257	Invalid sequence data feature in <221> in SEQ ID (227)
E 257	Invalid sequence data feature in <221> in SEQ ID (228)
E 257	Invalid sequence data feature in <221> in SEQ ID (230)

SEQUENCE LISTING

<110> Hengst den, Christiaan D.  
Gajic, Olivera  
Kuipers, Oscar P.  
Kok, Jan  
Sikkema, Jan  
Geurts, Johannes M.W.  
Nauta, Arjen

<120> Methods and means for regulating gene expression

<130> P63590US00

<140> 10562601  
<141> 2007-06-07

<150> US 10/562,601  
<151> 2005-12-28

<150> PCT/NL2004/000474  
<151> 2004-07-02

<150> EP 03077074.7  
<151> 2003-07-02

<160> 234

<170> PatentIn Ver. 3.3

<210> 1  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> CodY target sequence

<400> 1  
atgttcagaa aattcatgaa cat

23

<210> 2  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer sto 14

<400> 2  
cttgccatgg aatcacccg

19

<210> 3  
<211> 28

<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> primer opp1  
  
<400> 3  
gctctagaca ctcacttgg ttgcttcc

28

<210> 4  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> primer opp2  
  
<400> 4  
aactgcagga aaattcatga acataacc

27

<210> 5  
<211> 28  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> primer opp3  
  
<400> 5  
aactgcagta aaacaataat aaaagcag

28

<210> 6  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> primer opp4  
  
<400> 6  
aactgcagga taataaaatt tggactg

27

<210> 7  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> primer opp14  
  
<400> 7  
aactgcagcg taatgttcag aaaattc

27

<210> 8  
<211> 38  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer opp15 (a)

<400> 8  
aactgcagcg taatatttag aaaattcatg aacatacc

38

<210> 9  
<211> 38  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer opp15 (b)

<400> 9  
aactgcagcg tactgtgccg aaaattcatg aacatacc

38

<210> 10  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer cod280A

<400> 10  
gggaattcgg attgtctatc tgccctcg

27

<210> 11  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer cod280B

<400> 11  
gggggatcca gatctgacca tgattacgcc aagctt

36

<210> 12  
<211> 60  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer HC-5

<400> 12  
ctagaccacc atggggcata accatcacca tcacgtggct acattacttg aaaaaacacg 60

<210> 13  
<211> 37  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> primer HC-6

<400> 13  
ctagtctaga ttagaaatta cgtccagcaa gtttatac 37

<210> 14  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> inversely repeated (IR) cis-element

<400> 14  
aattttcwga aaatt 15

<210> 15  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> consensus sequence GTP binding motif in CodY homologs

<220>  
<221> Xaa  
<222> (2)..(2)  
<223> Arg

<220>  
<221> Xaa  
<222> (3)..(3)  
<223> Met, Gly, Ile, Lys, Gln

<220>  
<221> Xaa  
<222> (4)..(4)  
<223> Gly

<220>  
<221> Xaa  
<222> (5)..(5)  
<223> Thr

<220>  
<221> Xaa  
<222> (7)..(7)  
<223> Ser

<400> 15  
Gly Gly Glu Arg Leu Gly Thr Thr  
1 5

<210> 16  
<211> 8  
<212> PRT  
<213> Escherichia coli

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 16  
Leu Gly Gly Gly Thr Gly Thr Gly  
1 5

<210> 17  
<211> 8  
<212> PRT  
<213> Bacillus subtilis

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 17  
Gly Gly Glu Arg Leu Gly Thr Leu  
1 5

<210> 18  
<211> 8  
<212> PRT  
<213> Bacillus halodurans

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 18  
Gly Gly Gln Arg Leu Gly Thr Leu  
1 5

<210> 19

<211> 8  
<212> PRT  
<213> Clostridium difficile  
  
<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 19  
Gly Gly Met Arg Leu Gly Ser Leu  
1 5

<210> 20  
<211> 8  
<212> PRT  
<213> Clostridium acetobutylicum

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 20  
Asn Arg Glu Arg Leu Gly Thr Leu  
1 5

<210> 21  
<211> 8  
<212> PRT  
<213> Streptococcus pneumoniae

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 21  
Ser Gly Ile Arg Leu Gly Ser Leu  
1 5

<210> 22  
<211> 8  
<212> PRT  
<213> Enterococcus faecalis

<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 22  
Ala Gly Lys Arg Leu Gly Thr Ile  
1 5

<210> 23  
<211> 8  
<212> PRT  
<213> *Lactococcus lactis*  
  
<220>  
<221> BINDING  
<222> (1)..(8)  
<223> /note="Putative GTP binding motif G1"

<400> 23  
Ser Gly Met Arg Leu Gly Thr Phe  
1 5

<210> 24  
<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> consensus sequence GTP binding domain in CodY homologs

<220>  
<221> Variant  
<222> (2)..(2)  
<223> Ala, Lys

<220>  
<221> Variant  
<222> (3)..(3)  
<223> Phe, Ile

<400> 24  
Asp Arg Val Gly  
1

<210> 25  
<211> 4  
<212> PRT  
<213> *Escherichia coli*

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G3"

<400> 25  
Asp Ala Phe Gly  
1

<210> 26  
<211> 4

<212> PRT  
<213> *Bacillus subtilis*  
  
<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G3"

<400> 26  
Asp Arg Val Gly  
1

<210> 27  
<211> 4  
<212> PRT  
<213> *Clostridium difficile*

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G3"

<400> 27  
Asp Arg Ile Gly  
1

<210> 28  
<211> 4  
<212> PRT  
<213> *Lactococcus lactis*

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G3"

<400> 28  
Asp Lys Ile Gly  
1

<210> 29  
<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> consensus sequence GTP motif in CodY homologs

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<220>

<221> VARIANT  
<222> (3)..(3)  
<223> Leu, Phe, Asn, Ser, Gln

<400> 29  
Asn Lys Gly Asp  
1

<210> 30  
<211> 4  
<212> PRT  
<213> Escherichia coli

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 30  
Thr Ser Leu Asp  
1

<210> 31  
<211> 4  
<212> PRT  
<213> Bacillus subtilis

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 31  
Asn Lys Phe Leu  
1

<210> 32  
<211> 4  
<212> PRT  
<213> Bacillus stearothermophilus

<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 32  
Asp Lys Phe Leu  
1

<210> 33  
<211> 4  
<212> PRT  
<213> Clostridium difficile  
  
<220>  
<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 33  
Asn Glu Gly Ile  
1

<210> 34  
<211> 4  
<212> PRT  
<213> Clostridium acetobutylicum  
  
<220>

<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 34  
Ile Leu Asn Asp  
1

<210> 35  
<211> 4  
<212> PRT  
<213> Streptococcus pneumoniae  
  
<220>

<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 35  
Leu Ile Ser Asp  
1

<210> 36  
<211> 4  
<212> PRT  
<213> Enterococcus faecalis  
  
<220>

<221> BINDING  
<222> (1)..(4)  
<223> /note="Putative GTP binding motif G4"

<400> 36  
Asn Gln Gln Phe

<210> 37  
 <211> 4  
 <212> PRT  
 <213> *Staphylococcus aureus*  
  
 <220>  
 <221> BINDING  
 <222> (1)..(4)  
 <223> /note="Putative GTP binding motif G4"

<400> 37  
 Glu Lys Gly Ile  
 1

<210> 38  
 <211> 4  
 <212> PRT  
 <213> *Lactococcus lactis*  
  
 <220>  
 <221> BINDING  
 <222> (1)..(4)  
 <223> /note="Putative GTP binding motif G4"

<400> 38  
 Thr Gly Leu Phe  
 1

<210> 39  
 <211> 26  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> presence of the putative CodY box in *yreE*

<400> 39  
 taattttctg ataatatatgt caattt 26

<210> 40  
 <211> 26  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> presence of the putative CodY box in *ctrA*

<400> 40  
 taatttactg acaagtctgt cagtaa 26

<210> 41  
<211> 26  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> presence of the putative CodY box in yciC

<400> 41  
taatttactg acaaaaattat cagaac 26

<210> 42  
<211> 26  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> presence of the putative CodY box in optA

<400> 42  
aaattttctg acaataataa aaattg 26

<210> 43  
<211> 26  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> presence of the putative CodY box in optS

<400> 43  
aaattatcag aaaaatacaa caatat 26

<210> 44  
<211> 26  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> presence of the putative CodY box in optS

<400> 44  
taattttcag aataaatatga aaattc 26

<210> 45  
<211> 26  
<212> DNA  
  
<213> Artificial Sequence  
  
<220>  
<223> presence of the putative CodY box in parA

<400> 45  
taatTTactg atagatttgt cagtaa 26

<210> 46  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in aroF

<400> 46  
taatTTactg acagttctgt cagtaa 26

<210> 47  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in vacB1

<400> 47  
aaatTTactg acaaaaaaga taatgg 26

<210> 48  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in optA

<400> 48  
taatTTcag aaaacataac cattat 26

<210> 49  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in ypaG

<400> 49  
gaatTTtatg aaaaaaatat taattg 26

<210> 50  
<211> 26  
<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in yiaB

<400> 50  
gaatttactg acgaatctat cattaa 26

<210> 51

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in ysdC

<400> 51  
tcattctctg acaaatctgt cagtaa 26

<210> 52

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in hemK

<400> 52  
aaatttactg acaagcttgt tagtat 26

<210> 53

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in prfC

<400> 53  
aaatttaatg ataaaacaat tagttt 26

<210> 54

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in yugB

<400> 54  
aaagttactg acaaatctgt cagtaa 26

<210> 55  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in murD

<400> 55  
ttatTTactg acaagtctgt cagtaa

26

<210> 56  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in ywdG

<400> 56  
tattttactg acaaaaaaaat aagttt

26

<210> 57  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in parC

<400> 57  
taatTTactg acagctttgt cagtaa

26

<210> 58  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in pepC

<400> 58  
aaatTTactg acagagctgt cagtaa

26

<210> 59  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> presence of the putative CodY box in mutM

<400> 59

aaatttactg acagacttgt tagtaa

26

<210> 60

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in rgpAB

<400> 60

aaatttactg acaacttgt cagaag

26

<210> 61

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in vacB1

<400> 61

aaaatgtctg ataaaatgat taatac

26

<210> 62

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in recN

<400> 62

taatttactg acagaatttt aaattt

26

<210> 63

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> presence of the putative CodY box in llrH

<400> 63

aaaattacta acaaaaactgt tagtaa

26

<210> 64

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 64

aattttcaga aaatt

15

<210> 65

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 65

aattgtcaga aaatt

15

<210> 66

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 66

aattttctga taatt

15

<210> 67

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 67

aattttcaga taatt

15

<210> 68

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 68

atttttcaga aaatt

15

<210> 69

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 69  
aattttcgga aaaat 15

<210> 70

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 70  
aattttcaga aaata 15

<210> 71

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 71  
acttttcaga aaatt 15

<210> 72

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 72  
aattttctga atatt 15

<210> 73

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> motif in L. lactis MG1363 genome

<400> 73  
atttttcaga aaaat 15

<210> 74  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> motif in L. lactis MG1363 genome

<400> 74

aattgtcaga caatt

15